	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	10	DNA adj methylation adj inhibitor	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/27 10:44			0
2	BRS	L2	70	(DNA adj methylation) same inhibitor	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/27 10:45			0
3	BRS	L3	4815	decitabine or cytidine	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/27 10:45			0
4	BRS	L4	3	3 same (1 or 2)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/27 10:46			0
5	BRS	L5	62124	cancer same treat$4	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/27 10:47			0
6	BRS	L6	71	3 same 5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/27 10:47			0
7	BRS	L7	0	6 same (in adj vivo)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/27 10:48			0
8	BRS	L8	12	6 same (patient or animal or mammal)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/27 10:48			0

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FILE 'HOME' ENTERED AT 12:22:39 ON 27 NOV 2002

=> file medline caplus biosis embase scisearch agricola
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 12:23:07 ON 27 NOV 2002

FILE 'CAPLUS' ENTERED AT 12:23:07 ON 27 NOV 2002
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FILE 'AGRICOLA' ENTERED AT 12:23:07 ON 27 NOV 2002

=> s (DNA methylation) (p) inhibitor
L1        1779 (DNA METHYLATION) (P) INHIBITOR

=> s decitabine or cytidine
L2       32710 DECITABINE OR CYTIDINE

=> s l1 (p) l2
L3          63 L1 (P) L2

=> s cancer (p) treat?
L4      452248 CANCER (P) TREAT?

=> s l3 (p) l4
L5          12 L3 (P) L4

=> duplicate remove l5
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L5
L6             7 DUPLICATE REMOVE L5 (5 DUPLICATES REMOVED)

=> d l6 1-7 ibib abs

L6   ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:832643  CAPLUS
DOCUMENT NUMBER:          137:304765
TITLE:                    Compositions and methods for reestablishing gene
                          transcription through inhibition of DNA methylation
                          and histone deacetylase
INVENTOR(S):              Dimartino, Jorge
PATENT ASSIGNEE(S):       Supergen, Inc., USA
SOURCE:                   PCT Int. Appl., 54 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2002085400      A1   20021031       WO 2002-US12092  20020419
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
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PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2001-841744 A1 20010424
AB Compns. and methods are provided for ***treating*** diseases assocd. with aberrant silencing of gene expression such as ***cancer*** by reestablishing the gene expression through inhibition of DNA hypomethylation and histone deacetylase. The method comprises: administering to a patient suffering from the disease a therapeutically effective amt. of a ***DNA*** ***methylation*** ***inhibitor*** such as a cysteine analog such as ***decitabine*** , in combination with an effective amt. of histone deacetylase ***inhibitor*** such as hydroxamic acid, cyclic peptide, benzamide, butyrate, and depudecin.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:638131 CAPLUS
DOCUMENT NUMBER: 137:179872
TITLE: Restoring cancer-suppressing functions to neoplastic cells through DNA hypomethylation
INVENTOR(S): Rubinfeld, Joseph; Chang, Lucy; DiMartino, Jorge
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 14 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002114809	A1	20020822	US 2001-790483	20010221
WO 2002067681	A1	20020906	WO 2002-US4135	20020211

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-790483 A1 20010221
AB Compns. and methods are provided for ***treating*** diseases assocd. with abnormal cell proliferation such as ***cancer*** by storing inherent tumor-suppressing functions of neoplastic cells through DNA hypomethylation. The method comprises: delivering to a patient suffering from ***cancer*** a therapeutically effective amt. of a ***DNA*** ***methylation*** ***inhibitor*** such as ***decitabine*** , in combination with an effective amt. of an anti-neoplastic agent whose activity as an anti-neoplastic agent in vivo is adversely affected by aberrant ***DNA*** ***methylation*** . The anti-neoplastic agent can be an alkylating agent, an antibiotic agent, an antimetabolic agent, a retinoid, a hormonal agent, a plant-derived agent, an anti-angiogenesis agent and a biol. agent such as monoclonal antibody and interferon.

L6 ANSWER 3 OF 7 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002640331 IN-PROCESS
DOCUMENT NUMBER: 22286806 PubMed ID: 12399123
TITLE: Inactivation of p16(INK4a) expression in malignant mesothelioma by methylation.
AUTHOR: Wong Long; Zhou Joan; Anderson Daniel; Kratzke Robert A
CORPORATE SOURCE: Research Service, Minneapolis VA Medical Center, Minneapolis, MN, USA.
SOURCE: LUNG CANCER, (2002 Nov) 38 (2) 131-6.
Journal code: 8800805. ISSN: 0169-5002.
PUB. COUNTRY: Ireland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20021026
Last Updated on STN: 20021026

AB The molecular mechanisms of oncogenesis in mesothelioma involve the loss of negative regulators of cell growth including p16(INK4a). Absence of expression of the p16(INK4a) gene product is exhibited in virtually all mesothelioma tumors and cell lines examined to date. Loss of p16(INK4a) expression has also been frequently observed in more common neoplasms such as lung ***cancer*** as well. In a wide variety of these malignancies, including lung ***cancer*** , p16(INK4a) expression is known to be inactivated by hypermethylation of the first exon. In a survey of ten mesothelioma cell lines, one cell line (NCI-H2596) was identified as possessing loss of p16(INK4a) gene product following gene methylation. This methylation in these mesothelioma cells could be reversed, resulting in re-expression of p16(INK4a) protein, following the ***treatment*** of the cells with ***cytidine*** analogs, which are known ***inhibitors*** of ***DNA*** ***methylation*** . In previous clinical trials in mesothelioma, the ***cytidine*** analog dihydro-5-azacytidine (DHAC) has been found to induce clinical responses in approximately 17% of patients with mesothelioma ***treated*** with this drug, including prolonged complete responses. In addition, we identified evidence for methylation of p16(INK4a) in three of 11 resected mesothelioma tumor samples. When both cell lines and tumors are combined, inactivation of p16(INK4a) gene product expression following DNA hypermethylation was found in four of 21 samples (19%). We are further exploring the clinical significance of inhibition of methylation in mesothelioma by ***cytidine*** analogs. This may provide a potential ***treatment*** target in some mesothelioma tumors by inhibition of methylation.

L6 ANSWER 4 OF 7 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001161950 MEDLINE
DOCUMENT NUMBER: 21160236 PubMed ID: 11259619
TITLE: Activation of the p53 DNA damage response pathway after inhibition of DNA methyltransferase by 5-aza-2'-deoxycytidine.
AUTHOR: Karpf A R; Moore B C; Ririe T O; Jones D A
CORPORATE SOURCE: Division of Molecular Pharmacology, Huntsman Cancer Institute, University of Utah, Salt Lake City, Utah 84112, USA.
SOURCE: MOLECULAR PHARMACOLOGY, (2001 Apr) 59 (4) 751-7.
Journal code: 0035623. ISSN: 0026-895X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010425
Last Updated on STN: 20010425
Entered Medline: 20010419

AB Transcriptional silencing of tumor suppressor genes by ***DNA*** ***methylation*** occurs in ***cancer*** cell lines and in human tumors. This has led to the pursuit of DNA methyltransferase inhibition as a drug target. 5-Aza-2'-deoxycytidine [5-aza-CdR (***decitabine***)], a potent ***inhibitor*** of DNA methyltransferase, is a drug currently in clinical trials for the ***treatment*** of solid tumors and leukemia. The efficacy of 5-aza-CdR may be related to the induction of methylation-silenced tumor suppressor genes, genomic hypomethylation, and/or enzyme-DNA adduct formation. Here, we test the hypothesis that 5-aza-CdR ***treatment*** is perceived as DNA damage, as assessed by the activation of the tumor suppressor p53. We show that 1) colon tumor cell lines expressing wild-type p53 are more sensitive to 5-aza-CdR mediated growth arrest and cytotoxicity; 2) the response to 5-aza-CdR ***treatment*** includes the induction and activation of wild-type but not mutant p53 protein; and 3) the induction of the downstream p53 target gene p21 is partially p53-dependent. The induction of p53 protein after 5-aza-CdR ***treatment*** did not correlate with an increase in p53 transcripts, indicating that hypomethylation at the p53 promoter does not account for the p53 response. It is relevant that 5-aza-CdR has shown the greatest promise in clinical trials for the ***treatment*** of chronic

myelogenous leukemia, a malignancy in which functional p53 is often retained. Our data raise [redacted] hypothesis that p53 activation [redacted]ay contribute to the clinical efficacy and/or toxicity of 5-aza-CdR.

L6 ANSWER 5 OF 7 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000091410 EMBASE
TITLE: DNA methylation inhibitors in the treatment of leukemias, myelodysplastic syndromes and hemoglobinopathies: Clinical results and possible mechanisms of action.
AUTHOR: Lubbert M.
CORPORATE SOURCE: M. Lubbert, Department of Medicine, Division of Hematology/Oncology, Univ. of Freiburg Medical Center, Hugstetter Str. 55, D-79106 Freiburg, Germany. luebbert@mmll.ukl.uni-freiburg.de
SOURCE: Current Topics in Microbiology and Immunology, (2000) 249/-(135-164).
Refs: 103
ISSN: 0070-217X CODEN: CTMIA3
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB From results of clinical studies performed over more than 20 years with both azacitidine and ***decitabine*** in acute leukemias and MDS, one can conclude that both have comparable activity in these diseases. Relapsed and refractory AML and previously untreated high-risk MDS patients have been the most extensively studied subgroups with respect to drug schedule and effectivity. In relapsed/refractory AML (and CML in blast crisis), schedules with total doses ranging between 500 mg/m2 and 1500 mg/m2 with either drug are as effective (or are superior to) high-dose Ara-C. Lower dose schedules in the ***treatment*** of AML have been explored only in a limited number of studies, with inconclusive results regarding the best schedule and effectivity. The pioneering studies of the Aviano group have demonstrated the effectivity of several low-dose schedules in high-risk MDS (which often precedes AML of the elderly, since these patients often present with a clinical or morphologically detectable myelodysplastic phase). The majority of these AML patients are not eligible for intensive induction-consolidation ***treatment*** , due to their age and co-morbidity. Therefore, it would be of great interest to systematically study lower dose, first-line schedules of ***decitabine*** or azacitidine in this patient group. Outpatient schedules using subcutaneous injection would of course be very useful in this regard. The initial, rapid blast lysis that is typically induced by Ara-C often does not occur with methylation ***inhibitors*** . Therefore, combinations with hydroxyurea or Ara-C would probably be necessary to control clinically relevant leukocytosis present at the start of ***treatment*** . Kinetics of blast removal in the MDS trials show that these drugs are most effective when given over a prolonged period of repeated courses, which might be considered in the design of such protocols. Once the best response is achieved, ***DNA*** ***methylation*** ***inhibitors*** , given at even lower doses, may also be useful agents in the maintenance of these responses. The randomized phase-III study performed by the CALGB (SILVERMAN et al. 1998) has implicated azacitidine as a drug to alter the natural course of high-risk MDS. The very encouraging results of phase-II studies with ***decitabine*** also strongly urge for proof of its effectivity in a controlled study. Since about 50% of high-risk MDS patients do not respond to demethylating agents, rational drug combinations should be another step in further improving these results. Given the known myelotoxicity of these drugs in a disease presenting with cytopenias, clinically effective combinations with compounds that have little or no myelotoxicity are highly desirable. These may include HGFs and/or differentiating agents, such as all-trans retinoic acid which, as a single agent, probably has little activity in MDS, but may be more effective in the presence of ***decitabine*** due to upregulation of its receptor (COTE and MOMPARLER 1997). Since most MDS patients eventually relapse following ***treatment*** with azacitidine or ***decitabine*** , a prolongation of remission may possibly be achieved with a lower dose schedule as maintenance therapy. Other future studies might define a possible role of even lower dose schedules (with less myelotoxicity) in low-risk MDS and in

other disorders that are responsive to ***DNA*** ***methylation*** ***inhibitors*** . KOS[redacted]et al. (1998) recently reporte[redacted]hat ***decitabine*** , at starting doses of 1.5 mg/kg per course (divided into ten doses of 0.15 mg/kg administered over 14 days), augments HbF levels in sickle-cell anemia patients. Other recurrent effects seen at this very low dose were mild neutropenia and an increase in platelet count. The promising early results of this interesting study imply that this drug exerts its mechanism(s) even at a total dose that is .apprx.50% of that used in high-risk MDS (notwithstanding different time schedules of administration). Further studies are necessary to define this activity in sickle cell patients that are refractory to HU with respect to duration of ***treatment*** , development of resistance, and potential carcinogenicity. The ongoing studies by Giralt and coworkers on ***decitabine*** in the allogeneic transplantation setting show that it is feasible to use this drug in preparative regimens in leukemia and MDS patients. Since the relapse rate of AML and MDS patients in non-intensive preparative regimens is high, the use of this compound, which can upregulate MHC class-I molecules in residual malignant cells and, therefore, improve antileukemic effects of donor-lymphocyte infusion, should be further defined. The phase-I/II studies of azacitidine and ***decitabine*** performed in the 1970s and 1980s, respectively, in patients with solid tumors have yielded disappointing results overall. However, with the knowledge derived from studies of single-agent ***DNA*** - ***methylation*** ***inhibitors*** in MDS and AML regarding effective drug schedules, the very limited non-hematologic toxicity and the necessity to administer these drugs over a prolonged period to achieve a progressive removal of malignant cells, it would be of interest to re- evaluate the activity of these drugs in solid tumors. The rationale for revisiting this issue could possibly be strengthened by recent investigations from several laboratories demonstrating hypermethylation and transcriptional silencing of tumor-suppressor genes (p16/INK4A, p15/INK4B, Rb, VHL) in different types of solid tumors. Results obtained on decreased methylation of p15 in mononuclear bone marrow cells from MDS ***treated*** with ***decitabine*** suggest hypermethylated genes as appropriate targets of ***DNA*** ***methylation*** ***inhibitors*** even at non-intensive dose schedules. Given their short plasma half-life, repeated administration of ***decitabine*** or azacitidine with prolonged infusion duration in solid tumors with known hypermethylation of p16, e.g., bladder ***cancer*** of non-small-cell lung ***cancer*** , might result in antitumor activity that is superior to the disappointing results obtained with 1-h infusion schedules. The available data on the mechanism of action of these drugs strengthen the idea that it is different from that of agents that act primarily via their cytotoxic effects, such as low-dose Ara-C. In 1984, Momparler et al. described the effect of ***decitabine*** in leukemia as probably involving '... gene activation and induction of differentiation. One would not expect to observe an acute cell kill, but a disorganization of gene expression and a gradual decrease in cell number due to senescence.' In fact, most investigators ***treating*** patients with MDS with these drugs have observed remissions obtained in the absence of true bone marrow aplasia and late remissions occurring months after stopping administration of these drugs. Since hypermethylation and silencing of tumor-suppressor genes involved in cell-cycle regulation is frequent in leukemia and MDS, demethylation and reactivation of such genes might, at least in part, explain these phenomena. It is tempting to speculate what other groups of genes may be subject to demethylation in diseases that are responsive to ***DNA*** ***methylation*** ***inhibitors*** . Pinto has reported upregulation of granulocyte-colony-stimulating-factor receptor on bone marrow cells from a patient with MDS ***treated*** with ***decitabine*** (PINTO and ZAGONEL 1993), which would be an attractive, simple explanation for the observed improvement of granulocytopenia in responding patients. Similarly, improvement of anemia and rapid induction of thrombocytosis in this disease following ***treatment*** with ***DNA*** - ***methylation*** ***inhibitors*** could be speculated to be due to upregulation of lineage-specific receptor molecules. Clonality studies on granulocytes mobilized in responding MDS patients may clarify whether the activity of ***DNA*** ***methylation*** ***inhibitors*** is via differentiation induction. Finally, with further evidence that DNA demethylation induced by both drugs is linked to their clinical activities, combinations with other compounds inhibiting methylation but lacking myelotoxicity, such as antisense oligonucleotides inhibiting Dnmt1

(RAMCHANDANI et al. 1997), would be very interesting combinations in diseases where azacitidin[redacted]nd ***decitabine*** are ac[redacted]e.

L6 ANSWER 6 OF 7 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 1998:653467 SCISEARCH
THE GENUINE ARTICLE: ZZ632
TITLE: Interesting responses in patients with advanced nonsmall lung ***cancer*** after ***treatment*** with the ***DNA*** - ***methylation*** ***inhibitor*** , 5-aza-2'-deoxycytidine (***decitabine***)
AUTHOR: Momparler R L (Reprint); Ayoub J; Dionne J; Belanger K
CORPORATE SOURCE: HOP NOTRE DAME DE BON SECOURS, CTR ONCOL, MONTREAL, PQ H3T 1C5, CANADA; HOP ST JUSTINE, CTR RECH PEDIAT, MONTREAL, PQ H3T 1C5, CANADA
COUNTRY OF AUTHOR: CANADA
SOURCE: ANNALS OF ONCOLOGY, (SEP 1998) Vol. 9, Supp. [2], pp. 630-630.
Publisher: KLUWER ACADEMIC PUBL, SPUIBOULEVARD 50, PO BOX 17, 3300 AA DORDRECHT, NETHERLANDS.
ISSN: 0923-7534.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L6 ANSWER 7 OF 7 MEDLINE
ACCESSION NUMBER: 84113420 MEDLINE
DOCUMENT NUMBER: 84113420 PubMed ID: 6198436
TITLE: DNA modification, differentiation, and transformation.
AUTHOR: Jones P A; Taylor S M; Wilson V
CONTRACT NUMBER: 1-T32-CA90320 (NCI)
CA33592 (NCI)
GM25739 (NIGMS)
SOURCE: JOURNAL OF EXPERIMENTAL ZOOLOGY, (1983 Nov) 228 (2) 287-95.
Ref: 51
Journal code: 0375365. ISSN: 0022-104X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198403
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19840314

AB Substantial evidence has accumulated over the last 5 years that the methylation of cytosine residues in vertebrate DNA is implicated in the control of gene expression. We have used analogs of ***cytidine*** , modified in the 5 position, as specific ***inhibitors*** of ***DNA*** ***methylation*** to probe the relationship between this process and cellular differentiation. 5-Azacytidine effected marked changes in the differentiated state of cultured cells and induced the formation of biochemically differentiated muscle, fat, and chondrocytes from mouse fibroblast cell lines. Since the analog is a powerful ***inhibitor*** of ***DNA*** ***methylation*** , we suggest that this inhibition is causally related to the mechanism of phenotypic conversion. DNA extracted from cells ***treated*** with 5-azacytidine was hemimethylated and was used as an efficient acceptor of methyl groups in an in vitro reaction in the presence of eukaryotic methylases. In vitro methylation was inhibited if the substrate DNA was preincubated with a diverse range of chemical carcinogens including benzo(a)pyrene diolepoxide. Thus, chemical carcinogens may induce changes in gene expression by alteration of cellular methylation patterns. Recent experiments have also demonstrated that freshly explanted diploid fibroblasts from mice, hamsters, and humans lose substantial quantities of 5-methylcytosine during cell division and aging in culture. Taken together, these experiments suggest that the genomic distribution of 5-methylcytosine might have importance in normal differentiation and also in the aberrant gene expression found in ***cancer*** and senescence in culture.

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	27.52	27.73

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.24	-1.24

STN INTERNATIONAL LOGOFF AT 12:26:50 ON 27 NOV 2002

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1	BRS	L1	1771519	cancer or antineoplastic or carcinoma or scarcoma or myeloma or tumor or adenoma or adenocarcinoma or malignant or lymphoma or leukemia or melanoma	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/21 19:11			0
2	BRS	L2	70	(DNA adj methylation) same inhibitor	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/21 19:13			0
3	BRS	L3	4773	cytidine	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/21 19:13			0
4	BRS	L4	42	decitabine	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/21 19:13			0
5	BRS	L5	118	(histone adj deacetylase) same inhibitor	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/21 19:14			0
6	BRS	L6	65	(hydroxymic adj acid) or (trichostatin adj A) or pyroxamide or oxamflatin or (bishydroxamic adj acid) or (m-carboxy-cinnamic adj acid)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/21 19:17			0
7	BRS	L7	514	(trapoxin adj A) or apicidin or fr901228 or depsipeptide	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/21 19:18			0
8	BRS	L8	10585	benzamide or MS-27-275	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/21 19:19			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
9	BRS	L9	54259	butyrate or (butyric adj acid) or phenylbutyrate or (arginine adj butyrate)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/21 19:20			0
10	BRS	L10	1	depudecin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/21 19:20			0
11	BRS	L11	4857	2 or 3 or 4	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/21 19:21			0
12	BRS	L12	64062	5 or 6 or 7 or 8 or 9 or 10	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/21 19:21			0
13	BRS	L13	13	1 same 11 same 12	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/21 19:22			0

=> d his

(FILE 'HOME' ENTERED AT 19:31:41 ON 21 NOV 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
19:32:09 ON 21 NOV 2002
L1 5184193 S CANCER OR CARCINOMA OR SARCOMA OR TUMOR OR MALIGNANT OR LEUKE
L2 1777 S (DNA METHYLATION) (P) INHIBITOR
L3 32691 S CYTIDINE OR DECITABINE
L4 34371 S L2 OR L3
L5 3671 S (HISTONE DEACETYLASE) (P) INHIBITOR
L6 16304 S (HYDROXAMIC ACID) OR (TRICHOSTATIN A) OR OXAMFLATIN OR PYROXA
L7 4070 S (TRAPOXIN A) OR APICIDIN OR DEPSIPEPTIDE OR FR901228
L8 27241 S BENZAMIDE OR MS-27-275
L9 105163 S BUTYRATE OR (BUTYRIC ACID) OR PHENYLUTYRATE OR (ARGININE BUTY
L10 152314 S L5 OR L6 OR L7 OR L8 OR L9
L11 155 S L1 (P) L4 (P) L10
L12 95 S L11 (P) TREAT?
L13 27 DUPLICATE REMOVE L12 (68 DUPLICATES REMOVED)
L14 50 DUPLICATE REMOVE L11 (105 DUPLICATES REMOVED)
L15 23 S L14 NOT L13

=> log y

L13 ANSWER 18 OF 27 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 2001124267 MEDLINE
DOCUMENT NUMBER: 21028083 PubMed ID: 11156387
TITLE: Transcriptional activation of estrogen receptor alpha in human breast cancer cells by histone deacetylase inhibition.
AUTHOR: Yang X; Ferguson A T; Nass S J; Phillips D L; Butash K A; Wang S M; Herman J G; Davidson N E
CORPORATE SOURCE: The Johns Hopkins Oncology Center, Johns Hopkins University, Baltimore, Maryland 21231, USA.
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AB Recent findings have established a connection between ***DNA*** ***methylation*** and transcriptionally inactive chromatin characterized by deacetylated histones. Because the absence of estrogen receptor alpha (ERalpha) gene expression has been associated with aberrant methylation of its CpG island in a significant fraction of breast ***cancers*** , we tested whether ***histone*** ***deacetylase*** activity contributes to the transcriptional inactivation of the methylated ER gene in a panel of ER-negative human breast ***cancer*** cells. ***Treatment*** of these cells with ***trichostatin*** ***A*** , a specific ***histone*** ***deacetylase*** ***inhibitor*** , led to dose- and time-dependent re-expression of ER mRNA as detected by reverse transcription-PCR without alteration in ERalpha CpG island methylation. ***Trichostatin*** ***A*** -induced ER re-expression was associated with increased sensitivity to DNase I at the ER locus in MDA-MB-231 cells. These data implicate inactive chromatin mediated by histone deacetylation as a critical component of ER gene silencing in human breast ***cancer*** cells. Therefore, histone deacetylation may be a potential target for therapeutic intervention in the ***treatment*** of a subset of ER-negative breast ***cancers*** .

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L13 ANSWER 19 OF 27 MEDLINE DUPLICATE 13
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TITLE: Epigenetic regulation of androgen receptor gene expression in human prostate cancers.
AUTHOR: Nakayama T; Watanabe M; Suzuki H; Toyota M; Sekita N; Hirokawa Y; Mizokami A; Ito H; Yatani R; Shiraishi T
CORPORATE SOURCE: Second Department of Pathology, Mie University School of Medicine, Japan.
SOURCE: LABORATORY INVESTIGATION, (2000 Dec) 80 (12) 1789-96.
Journal code: 0376617. ISSN: 0023-6837.
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AB Epigenetic mechanisms including ***DNA*** ***methylation*** and histone deacetylation are thought to play important roles in gene transcriptional inactivation. Heterogenous expression of androgen receptor (AR), which appears to be related to variable responses to endocrine therapy in prostate ***cancer*** (PCa) may also be due to epigenetic factors. The methylation status of the 5' CpG island of the AR in 3 prostate ***cancer*** cell lines and 10 primary and 14 hormone-refractory PCa samples was determined using the bisulfite PCR methods. In DU145, CpG-rich regions of the AR were hypermethylated. By an immunohistochemical analysis, only one PCa sample had no AR expression, the others being heterogenous. Bisulfite sequencing and